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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/690,198	10/16/2000	Douglas A. Collins	COP1002	2250

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06/03/2002

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EXAMINER

WILLIS, MICHAEL A

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 06/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s)

09/690,198

Examiner

Michael A. Willis

Applicant(s)

COLLINS ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-120 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,7,9,12-15,18,20-24,49-51,55,56,60 and 61 is/are rejected.
- 7) ☒ Claim(s) 111 and 112 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 October 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2,4,6,8,10,11,16,17,19,21-23,25-48,52-54,57-59,62-110 and 113-120.

DETAILED ACTION

Election/Restrictions

1. Applicant's response of 11 February 2002 is entered as Paper No. 11. Applicant elects the invention of Group I, claims 1-112. Claims 113-120 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant further elects the species of doxorubicin-cobalamin conjugate described in example 1 of the specification. Claims 2, 4, 6, 8, 10-11, 16-17, 19, 21-23, 25-48, 52-54, 57-59, and 62-110 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim.

Drawings

2. Figure 1 is objected to because it contains errors in the structure of cobalamine. The substituent X is incorrectly drawn as having a double bond to the corrin ring. The correct structure should have the double bond attached to the N that is adjacent to the X substituent. Also, the use of CO₄ is confusing. The cobalt atom should be indicated by Co. Also, the amidoalkyl group indicated at position g in Figure 1 appears to have an extraneous covalent bond to a methyl group on the corrin ring. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

3. Claims 111 and 112 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3, 5, 7, 9, 12-15, 18, 20-24, 49-51, 55-56, and 60-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected for citing the Drawings in the claims. Claims are to be complete in themselves. See MPEP 2173.05(s).

6. Claim 18 is rejected for depending from non-elected claim 17.

7. Any remaining claims are rejected for depending from indefinite base claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 12-15, 18, 24, 49-51, 55, and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Pinson et al ("Synthesis of Two Doxorubicin-Cobalamin Bioconjugates" Ninth International Symposium on Recent Advances in Drug Delivery Systems, February 1999, pages 228-229). Pinson discloses doxorubicin-3-aminocobalamin compounds that are connected via a glutarate linker. While the disclosure of Pinson does not anticipate the elected species containing a leucine linker, the claims are rejected insofar as they generically read on doxorubicin-cobalamin conjugates.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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12. Claims 1, 3, 5, 7, 9, 12-15, 18, 20, 24, 49-51, 55-56, and 60-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smeltzer et al ("Cytotoxicities of Two New Cobalamin Bioconjugates" Ninth International Symposium on Recent Advances in Drug Delivery Systems, February 1999, pages 232-33) in view of Grissom et al (WO 98/08859; see US Pat. 6,315,978 for US Patent equivalent).

13. Smeltzer teaches the use of cobalamin bioconjugates as a delivery agent for doxorubicin. The cobalamin can be linked to doxorubicin without disrupting the binding of the vitamin to transport proteins (see introduction). The bioconjugates are shown to be less toxic than unmodified doxorubicin. Smeltzer clearly indicates that the essential components of the bioconjugates are doxorubicin and cobalamin.

14. Grissom teaches bioconjugates of organocobalt compounds and the delivery of bioactive agents. Grissom clearly teaches that the drug and cobalt components of the bioconjugates are connected via a spacer element (see col. 10, lines 26-40 of US 6,315,978). Grissom teaches that the nature of the spacer is not critical to the invention, and that a skilled artisan will readily recognize other spacers which can be used to link bioactive and cobalt components of the bioconjugates.

15. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the compounds of Smeltzer by the use of leucine as a linker due to Grissom's teachings that the nature of the linker is not critical to the practice of the invention.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1, 3, 5, 7, 9, 12-15, 18, 20, 24, 49-51, 55-56, and 60-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/027,593.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application claims cobalamin conjugates linked to therapeutic agents such as doxorubicin via amino acid linkers (see also Example 19 of the copending application).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cannon et al ("Synthesis and Uptake of a Radiolabeled


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cobalamin bioconjugate" Ninth International Symposium on Recent Advances in Drug Delivery Systems, February 1999, pages 230-31) is cumulative to the references cited above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael A. Willis whose telephone number is (703) 305-1679. The examiner can normally be reached on alternate Mon. and Tues. to Fri. from 9am-6:30 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.



Michael A. Willis
Examiner
Art Unit 1617

May 31, 2002



MICHAEL G. HARTLEY
PRIMARY EXAMINER